Remarks

Claims 1-15 are pending in the referenced case. Claims 1, 2, 6 and 9-11 were examined by the Examiner in the instant case. Claims 3-5 and 7-8 were previously restricted. Claims 12-15 are presently restricted. Applicant respectfully requests that claims 1, 2, 6 and 9-15 be allowed based on the following arguments.

Rejections under §112

Claims 1 and 6 are rejected under 35 U.S.C. §112, first paragraph, as failing to comply with the enablement requirement. The Examiner states that "an *in vitro* system is over-simplified compared to the body of a mammal and is not predictive of, nor correlate with the complex nature immune systems in humans. Due to the highly complex nature of immunology, extrapolating from *in vitro* models to mammals without *in vivo* validation is hazardous, likewise extrapolating results from one antigen to a non-analogous antigen is unpredictable." The Examiner concludes that one skilled in the art would be burdened with an undue quantity of *in vivo* experiments in order to make and use the current invention.

Thus, the crux of the Examiner's argument is that *in vitro* experimentation is not correlative of *in vivo* success, and experiments using one type of antigen do not provide enablement for other types of antigens. Regarding *in vitro* experimentation, there is clear precedent that *in vitro* data is sufficiently predicative for *in vivo* implementation for patentability purposes. See MPEP 2164.02; *In re Brana*, 51 F.3d 1560. In fact, there is a presumption in favor of Applicant that *in vitro* experiments are correlative to *in vivo* results. Id. This presumption can be rebutted by the Examiner with evidence to the contrary, but the Examiner's assertions that "*in vitro* systems are over-simplified compared to the body of a mammal" go to the very nature of the difference between *in vivo* and *in vitro*, not to why Applicant's specific *in vitro* experiment is inappropriate. Thus, the Examiner has not met her burden.

Regardless of the burden, however, Applicant believes that the Examiner is incorrect. Applicant's method is essentially directed to a novel adjuvant, i.e., a medium used to boost the results of an already known vaccine antigen. The protocols of administering the vaccine antigen are known in the art. The adjuvant is for a medicative boost of the vaccine antigen, and are correlative *in vitro* to *in vivo*.

Further, the Examiner seems to be confusing the requirements under the law for obtaining a patent with the requirements for obtaining government approval to market a particular drug for human consumption. See *Scott v. Finney*, 34 F.3d 1058 (Fed. Cir. 1994).

The stage at which an invention in this field becomes useful and worthy of patent protection is often well before it is ready to be administered to humans. As a result, the Examiner is placing undue import on what she feels is a lack of "clinical efficacy" of the LCM, when such a concern is more relevant to the FDA than the Patent Office. Therefore, the assertions of lack of enablement based on lack *in vitro* examples without *in vivo* validation is erroneous.

Moving onward, as stated above, the Examiner believe that the extrapolation from one antigen to another antigen is unpredictable. However, Applicant provides ample experiments and data to show that the LCM of the invention substantially influences immature to change into into mature, more effective antigen presenting cells. See specification pages 11-15. Antigen presenting cells, by there nature, can present varying types of antigens. Dendritic cells, in particular, have an extremely broad variety of antigens they can present, including prostate specific antigens. Thus the specification provides an enabling disclosure on how to enhance an immune response by improving the functionability of antigen presenting cells, wherein the antigen presenting cells by their nature are able to present prostate specific antigens. The tetanus toxoid experiment demonstrated that the antigen presenting cells have improved functionability under the method of the invention. This readily enables use of the LCM with other types of antigens simply by the process of switching the antigen. Essentially, the method can be readily used with any of the antigens of claims 3-8, as shown on page 8 of Applicant's specification, which also provides further evidence why the restriction requirements of the previous and prior action are improper.

As a conclusion, the Examiner states, "considering the lack of data or working example in the specification, the broad scope of the claims, and the complex state and unpredictable nature of the art," there is lack of enablement due to undue experimentation. The Examiner has cited In re Wands factors 3, 7 and 8. However, as shown above, citing of lack of working example based on the complex state of the art is improper. The remaining factor, the broad scope of the claims, is best analyzed under the auspices of §102 and 103, below. Therefore, claims 1 and 6 are believed patentable in view of §112.

Claim 1 Rejected under §102

The Examiner rejected Claims 1 under 35 USC 102(a) as being anticipated by Baxevanis et al. Applicant respectfully asserts that Baxevanis et al. does not disclose, teach or suggest all of the elements of independent Claim 1 and therefore does not anticipate the claims.

Specifically, Baxevanis is directed to a method that discloses the ability of anti-CD3 monoclonal antibodies to induce cytotoxic responses. The method includes deriving supernatants from donor PBMCs cultured with anti-CD3 mono-clonal antibodies (ADC3S) and administering the ACD3S into a patient to enhance the patients PBMC cytotoxicity. See Baxevanis, column 2, lines 10 onward. However, Baxevanis does not disclose administering the supernatant to a patient with the antigen against which the immune response is directed. In contrast, Applicant's claim 1 discloses a method for enhancing an immune response to an antigen in a mammal comprising "administering lymphocyte conditioned media **in combination with a vaccine of said antigen** to said mammal."

This view is further supported in Applicant's specification beginning at page 7, line 16 wherein lymphocyte conditioned medium is described as an adjuvant that enhances the function of a vaccine antigen. Even the title of Applicant's specification supports this position.

As there is no vaccine for an antigen administered to a patient in Baxevanis, Baxevanis does not disclose every element of Applicant's claim 1 and §102 is not applicable. In view of the foregoing, reconsideration and allowance of Claim 1 is respectfully requested.

Claims 1 and 2 Rejected under §103

The Examiner rejected Claims 1 and 2 under 35 USC 103(a) as being unpatentable over Baxevanis et al. in further view of Santamaria et al. Applicant respectfully asserts that the combination of Baxevanis and Santamaria, when considered separately or together, do not render Applicant's claims 1 and 2 obvious.

Baxevanis is cited for the above, and further cited for teaching immoblizing anti-CD3 monoclonal antibodies to culture PBMCs. Santamaria is further cited for disclosing the use of anti-CD3 coated beads.

In response, Applicant first restates that Baxevains does not disclose a method for enhancing an immune response to an antigen in a mammal comprising "administering lymphocyte conditioned media **in combination with a vaccine of said antigen** to said mammal," as disclosed in Applicant's claim 1. Santamaria, does not cure this problem, as it similarly does not disclose administering LCM in combination with a vaccine. In order to find obviousness, the combination of the cited references must include each and every element of Applicant's claims. See *In re Zurko*, 258 F.3d 1379, 1386 (Fed. Cir. 2001). Therefore, the combination of Baxevanis and Santamaria does not render the instant claim 1 obvious, and §103 is not applicable.

Further, Applicant notes that both Baxevanis and Santamaria disclose culturing PBMCs with anti-CD3 but not anti-CD28. In contrast, Applicant's claim 2 recites a method wherein the LCM is "derived from naïve T cells **cultured with anti**CD3/**CD28**-coated beads." This difference is not insignificant. The cytokine/chemokine products produced by stimulation of PBMC with antiCD3 and antiCD28 are clearly different from PBMC stimulated with antiCD3 alone. Compare, for example, Table 2 of Applicant's specification (page 14) with Table 2 of Baxevanis (page 1076). It is clear that activation of PBMC through both antiCD3 and CD28 is different than when exposed to antiCD3 alone.

As neither cited reference includes activation of PBMCs with antiCD28, the combination of the cited references do not include each and every element of Applicant's claims. Therefore, the combination of Baxevanis and Santamaria does not render the instant claim 2 obvious, and §103 is not applicable. In view of the foregoing, reconsideration and allowance of Claims 1 and 2 are respectfully requested.

Claims 1 and 9-11 Rejected under §103

The Examiner rejected Claims 1 and 9-11 under 35 USC 103(a) as being unpatentable over Baxevanis et al. in further view of Setaluri et al. Applicant respectfully asserts that the combination of Baxevanis and Setaluri, when considered separately or together, do not render Applicant's claims 1 and 9-11 obvious.

Baxevanis is cited for the above. Setaluri is cited for teaching dosage calculation and administration of a tumor antigen hourly, daily, weekly, monthly or yearly, by intramuscular or intravenous injection.

Applicant does not assert claims 9-11 to be separately patentable apart from their dependency on claim 1.

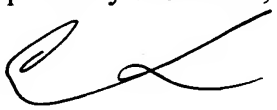
Restriction of claims 12-15

The Examiner restricts claims 12-15 for being directed to products that are different than the method in claim 1-11. The Examiner states that the "claimed method can be practiced with other materially different products such as Freud's adjuvant." The Examiner seems to have mischaracterized the invention. Claim 1 discloses a method of using an adjuvant, essentially, the method of using the adjuvant of claims 12-15. Claim 1 would not be practiced with Freud's adjuvant unless a user had an untaught desire to do so. Therefore, there restriction requirement is improper.

CONCLUSION

In conclusion, Applicant respectfully submits that Claims 1-2, 6, 9-11 and 12-15, are patentable in view of the references cited.

Respectfully submitted,



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